

to be mediated by chain reactions; (e) passive or narcotized nervous tissue consumes considerable oxygen simply to maintain itself, and the increase during activity is slight as compared to muscular tissue; (f) it is questionable whether the same mechanisms of oxidation function in surviving brain as in the intact animal;<sup>6</sup> and (g) the study of tissue *in vitro* yields a partial picture only, in any case, since general humoral effects are absent.

Thus, while isolated tissue work on surviving brain is yielding much sound biochemical information, as to oxidative mechanisms present, the effects of agents such as potassium, phosphate, or vitamin B, and the availability of different substrates, the difficulties of obtaining significant pharmacologic data are such that perhaps little real progress can be made for some time. Meanwhile, such studies as those of Meyer and his coworker<sup>7</sup> point out interesting relationships between physical properties of agents and their narcotic potency, suggesting an explanation of narcosis which may be less mysterious than the postulated selective inhibitory action of narcotics on the lactic dehydrogenase of certain ill-defined centers.

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#### AUTOCYTOTOXIC "ANTIBODIES?"

Among the speculative immunologic theories of current interest, none is of wider clinical application than the tentative hypothesis that certain progressive degenerative diseases of highly specialized parenchymatous tissues are due to an auto-immunologic, or auto-allergic vicious circle. This theory assumes that, as a result of an initial toxic or infectious injury, certain highly specialized organ-specific tissues colloids are so denatured as to render them specifically antigenic for their animal of origin. The resultant antiorgan-specific immunity may conceivably be due to "antibodies" specifically cytotoxic for normal homologous tissues. These autocytotoxins may conceivably be formed in sufficient amounts to cause perversion or suppression of homologous tissue function, with ultimate atrophy or degeneration.

This futuristic theory is an apparently logical deduction from the rapidly increasing number of organ-specific proteins, lipoids, and carbohydrates now recognized in animal tissues. Some of these specific organic products are known to require but slight chemical or physicochemical alteration to render them specifically antigenic for the same animal species.

Hektoen and Schulhof,<sup>1</sup> for example, found that the organ-specific proteins of the crystalline lens of the rabbit eye are not demonstrably antigenic for rabbits, causing the production of no de-

monstrable antilens precipitins. Burkey, Woods, and Woodhall,<sup>2</sup> however, found that normal rabbit lens proteins can be separated into three crystalline factors, one of which is highly antigenic for rabbits, if freed from the "inhibiting" action of the other two factors. The "fractional antibodies" thus formed may presumably reach a sufficiently high titer in actively immunized rabbits to cause autocytotoxic cataract.

One would suspect from this finding that certain local bacterial infections might so denature the organ-specific factors in the liver, kidney, thyroid gland, and central nervous system, for example, as to set up a similar immunochemical vicious circle, leading to progressive degenerative lesions of these organs. The latest apparent confirmations of this fear are the production, by Doctors Rivers and Schwenather<sup>3</sup> of the Rockefeller Institute, of progressive degenerative lesions of the central nervous system as a result of heterophile antibrain immunization.

Doctors Rivers and Schwenather gave eight monkeys repeated intramuscular injections with normal rabbit brain emulsions alternated with normal rabbit brain lipoids. Brain lipoids are known to be organic-specific haptens, which are rendered auto-antigenic by adsorption on an appropriate colloidal "carrier." After forty or more injections with these heterophile brain antigens, seven of Doctor Rivers' actively immunized monkeys began to show signs of ataxia. The ataxia became progressively worse and in certain cases ended in definite paralysis. Histologic study showed marked degenerative lesions of these ataxic or paralytic monkey brains, accompanied by extensive local demyelination.

The New York investigators, however, very carefully avoid a definite conclusion as to the probable immunochemical mechanism involved in this experimental encephalomyelitis. They did rule out, however, the possibility that the encephalomyelitis is due to an intercurrent infection. No bacteria were demonstrable in the degenerated brains, nor were they demonstrably infectious on intracerebral injections into normal monkeys, rabbits, guinea-pigs, or mice. The possibility that the encephalomyelitis might be due to an environmental virus, nonpathogenic for normal animals, but pathogenic for animals subjected to the repeated toxic injury incident to heterophile immunization, has not yet been tested.

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<sup>2</sup> Burkey, E. L., Woods, A. C., and Woodhall, M. B.: Arch. Ophth., 9:446, 1933.

<sup>3</sup> Rivers, T. M., and Schwenather, F. F.: J. Exper. Med., 61:689 (May), 1935.

<sup>6</sup> Ashford, C. A., and Dixon, K. C.: Biochem. J., 29:167, 1935.

<sup>7</sup> Meyer, K. H., and Hemmi, H.: Biochem. Z., 277:39, 1935.

<sup>1</sup> Hektoen, L., and Schulhof, K.: J. Infect. Dis., 34:433, 1924.

Sickness is very wasteful of time and money, as well as a disagreeable and alarming experience. It cuts off income and increases expenses. It threatens all that we hold most worth while—our ambitions, careers, usefulness to the community; our homes, friends, and families. It is the greatest obstacle to a serene, happy, contented, useful life.—Franklin D. Roosevelt.